

—
Fig.

1 CCCACGGCTC CGCATAAATC AGCACGGCC CGGAGAACCC CGCAATCTCT CGTACTTTAA GGCTGAAAC
 GGGTGGCAG GCGTATTAG CGCTCTGGG GCCTCTGGG GCGTTAGAGA CGGGGGTGT TTATGGCT AGATGAAATT CCCGACTTTG
 101 CCACGGGCCT GAGAGACTAT AAGAGCCGTT CCTACGCCA TGGAACAAACG GGCACAGAAC GCCCCGGCC
 GGTGGCGGA CCTCTCTGATA TTCTCGCAAG GGATGGGGT ACCTTGTTGC CCGTGTCTTG CCCCCGGG
 1 etgluglnar gglylnash AlaProAla1 aArgly1a1 HisGlyProGly
 201 GACCCAGGGA GGGGGGGGA GCCAGGGCTG GGCTCCGGGT CCCCAAGAAC ACCCTGGCTTG GGGTTCTGG
 CTGGGTCCT CGGGCCCT CGGTCGGAC AACACGAGC AACAGGGCG AACAGAGTC GACTCAGAC
 22 PROArg1 uAlaArgGly AlaArgProGly LeuValLeu 1ProLysThr LeuValSer1 aValAla1 aValLeu1 LeuValSer1 laGlusera1
 301 TCTGATCACC CAACAGGACC TAGCTCCCA CGAGAGGGCG GCCCCAAC AACAGGGTC CAGGCCCTCA
 AGACTAGTCG GTTGTCTGG ATCGAGGGT CGTCTCTGG CGGGGTGTT CTTCTCCAG GTCCGGGAGT
 55 LeuIleThr GlnglnAsp1 euAlaProG1 nGlnArgAla AlaProGln1 InLySArg1 rSerProSer
 401 TCAAGAGACG GTAGAGATTC CATCTCCCTG AAATATGGAC AGGACTATAG CACTCACTG AATGACCTCC
 AGTCTCTGCA CATCTCAAC GTAGAGGAC TTATACCTG TCCGTATATC GTGAGTGACC TTACTGGAGG
 88 sergluAsp1 LyArgAspC sIleSerCys Lystyrgly1nAspTyrSe rThrHistP AsnAspLeu1 eupheCysLe
 501 CAGGTGAAGT GGAGCTAAGT CCTCTGGCCA CGACCAAGAA CACAGTGT CAGTGGCAAC
 GTCCCACTCA CCTCGATTCA GGACGTTGT GCTGGTCTT GTGTCAACA GTCAAGGCTT
 122 GlyluVya 1GluLeuser ProCysThr1 hrThrArgas nThrValCys1 GlyAspCyst hrProTrpSe
 601 GAACTGCCG ACAGGGGTG CCTCTGGCCA GGTCAAGGTC CCAGCTGGG
 CTTCAAGGG TGTCGATTCA GGTCGACAG CCAGTCCCA
 155 LysCysArg ThrglyCysP roArgGlyMe tVallySva1 ValAlaValP heValCysLy
 701 GGAGTCACG TTGGCAGGGT AGTCTTGATT GTGCTGT
 CCTCAAGGG TGTCGACAG TCAGAACTAA CACCGACACA
 188 GlyValThr alaAlaAla1 ValLeu1 ValAlaValP heValCysLy
 801 GTGGCTGTG CGACCCGTG CCGTGGGACA AACGCTCACA
 CACCAACC CCTGAGTC AACGTCGGCA
 222 Glygly1 YasProGlu ArgValAsp1 rgserserg1 uProAlaGlu1 uvalGln1
 901 GGTCCCTGAG CAGGAATGG AAGTCCAGGA CCCAGCAGAG
 CCAACCTGGG CCACACCTCTT CTTAGGTCTG
 255 ValProGlu GlnglnMetG 1uvalGln1 uProAlaGlu1
 1001 GCTGAAAGGT CTCAGAGGAG GAGGCTGCTG GTTCCAGCAA ATGAAAGTGA
 CGACTTCCA GAGTCCTCCTC CGTCGAGGAC
 288 AlagliuAarg1 erglalarg1 gargLeu1 ValProAla1
 1 Incyspeas Paspheala Aspleuvalpro

Fig. 1 (cont.)

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Fig. 2 A

1 MEQRGONAPAAASGARKRHEGPGPREARGARPGLRLVPKTKTLVVAAVLLVSAESALITQQD
61 LAPQORAAPQQKRSSPSEGICPPGHHTISEDGRDCISQKYGQDYSTHWNDLLEFCLRCTRQD
1121 SGEVELSPCTTTRNTVCQCEGTFREEDSPEMCRKQRTGCQPRGMVKVGDTCPWSDIECVH
1181 KESGLITIGVTAAVVLLIVAFVCKSLIWWKKVLPYLGICSGGGGDPERVDRSSQRPGQAED
2241 NVLINEIVSILQOPTQVPEQEMEVQEPAEPTGVNMMLSPGESEHLLPEAEAERSORRRLVPA
3301 NEGDPTEETLRQCDDFDADLVPFDSWEPLMRKLGLMDNEIKVAKAEAAGHRTDTLYTMLIKW
3361 VNKTGRDASVHTLLDALETIGERLAKQKIEDHILLSSGGFMYLEGNADSALS

Fig. 2 B

APO2	FADD	LIVEDS	EPLM	RKIGT	M DNE	T KVA	AAZ	- -	G H R D T U
DR4	FAN1	VIVED	SNDQ	LMQ	Q IDU	T KNE	D Y R G T A	- -	G P G D A Y
APO3/DR3	VM	AAARR	Y	Y	Y	Y	Y	Y	Y
TNFR1	VENY	VPLR	Y	Y	Y	Y	Y	Y	Y
Fas/Apo1	INGV	MTLSQVNG	Y	Y	Y	Y	Y	Y	Y

APO2
 DRA
 APO3/DR3
 TNFRI
 Fas/Apol

Fig. 3

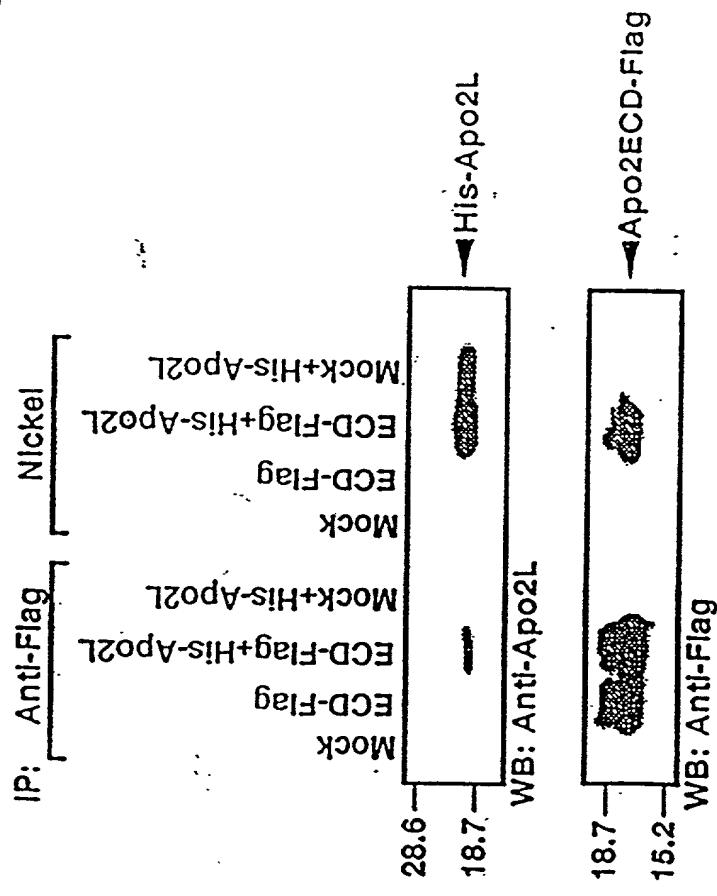
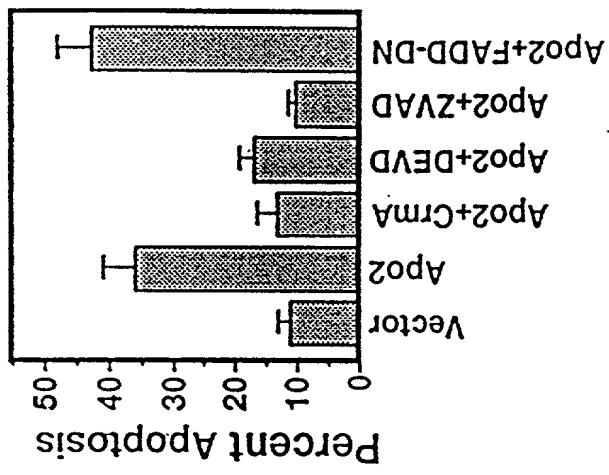
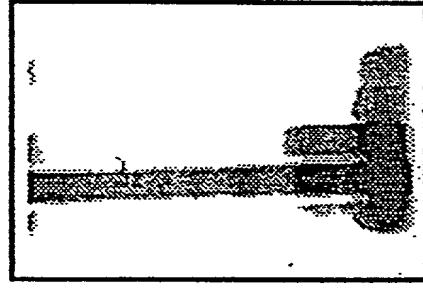


Fig. 4

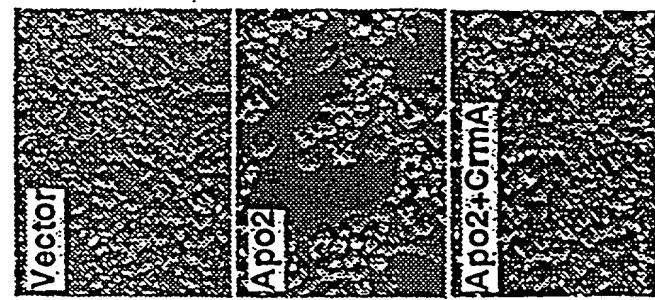
4C



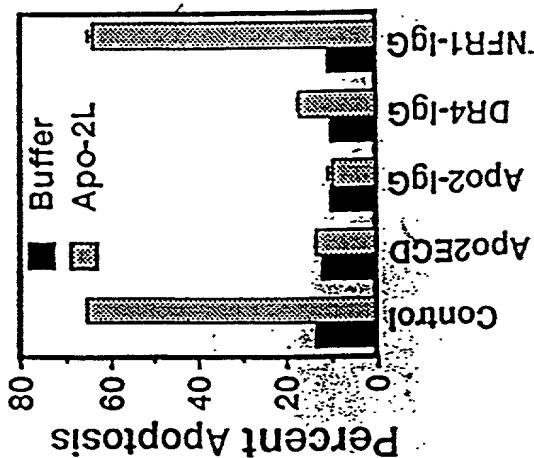
4B



4A



4D



4E

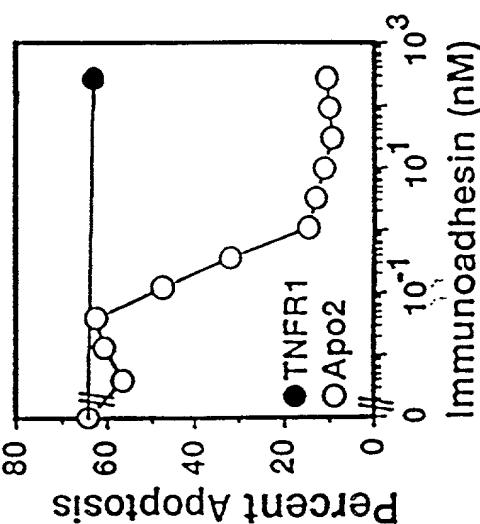


Fig. 5

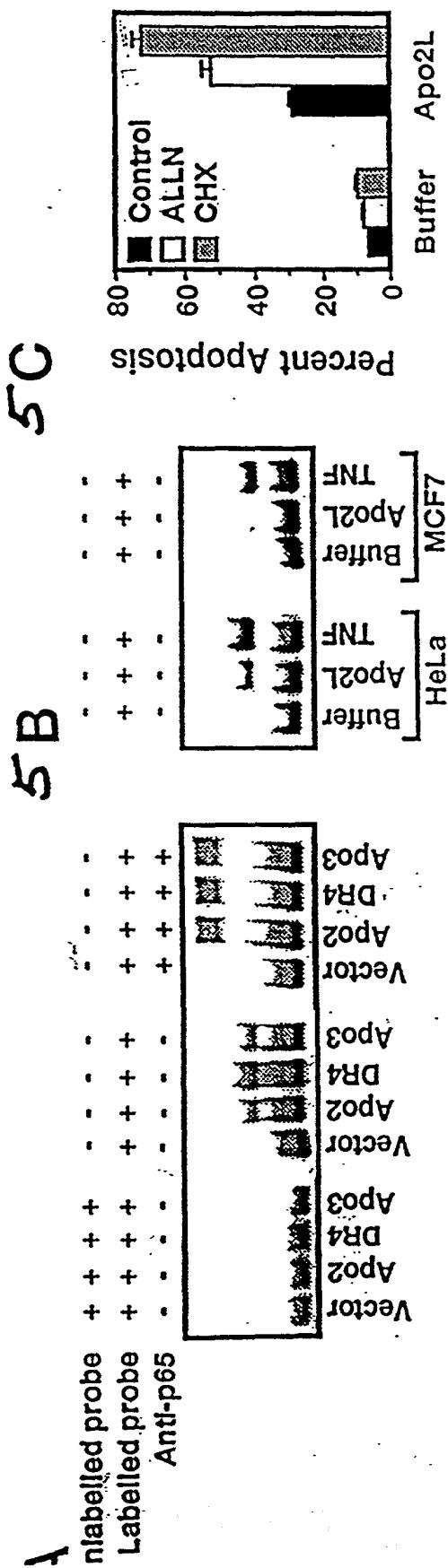
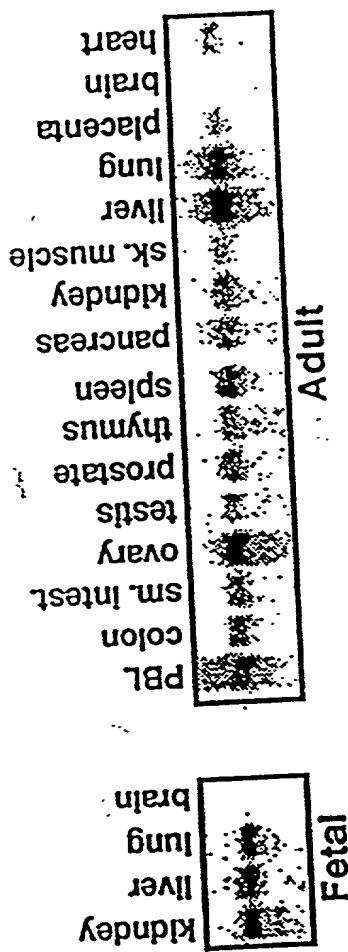
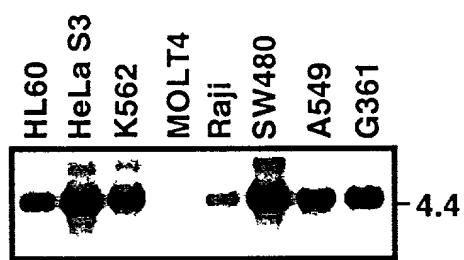


FIG. 6A





Cancer cell line

Fig. 6B

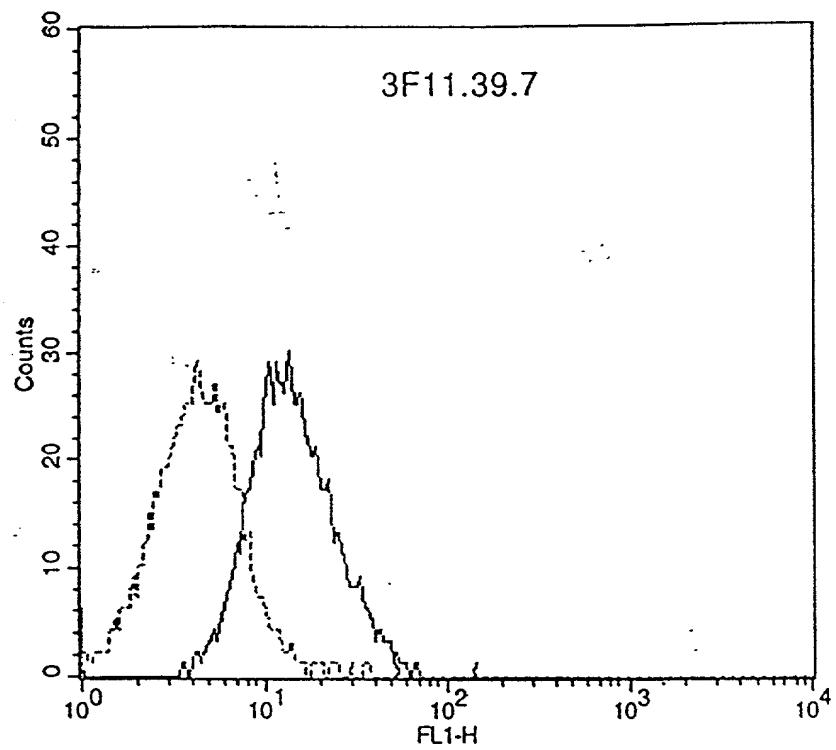


Fig. 7

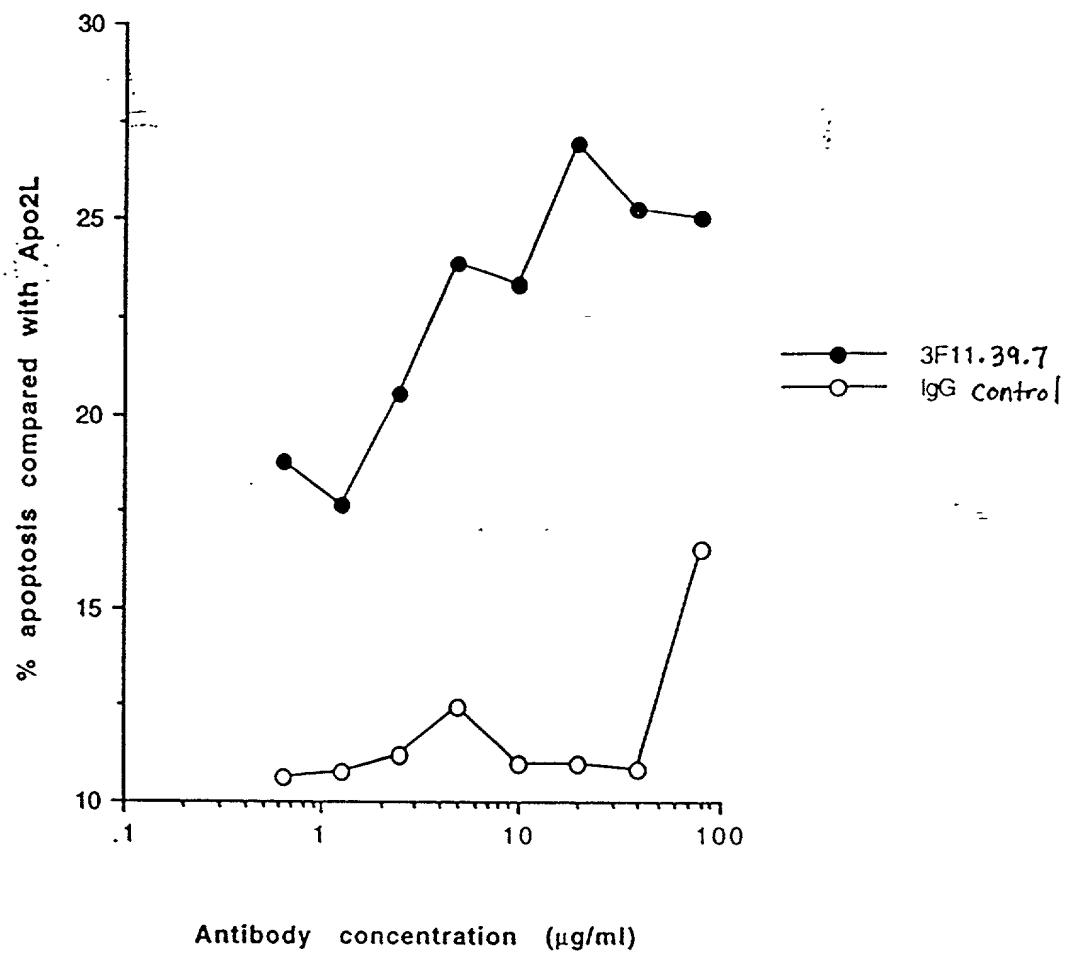


Fig. 8

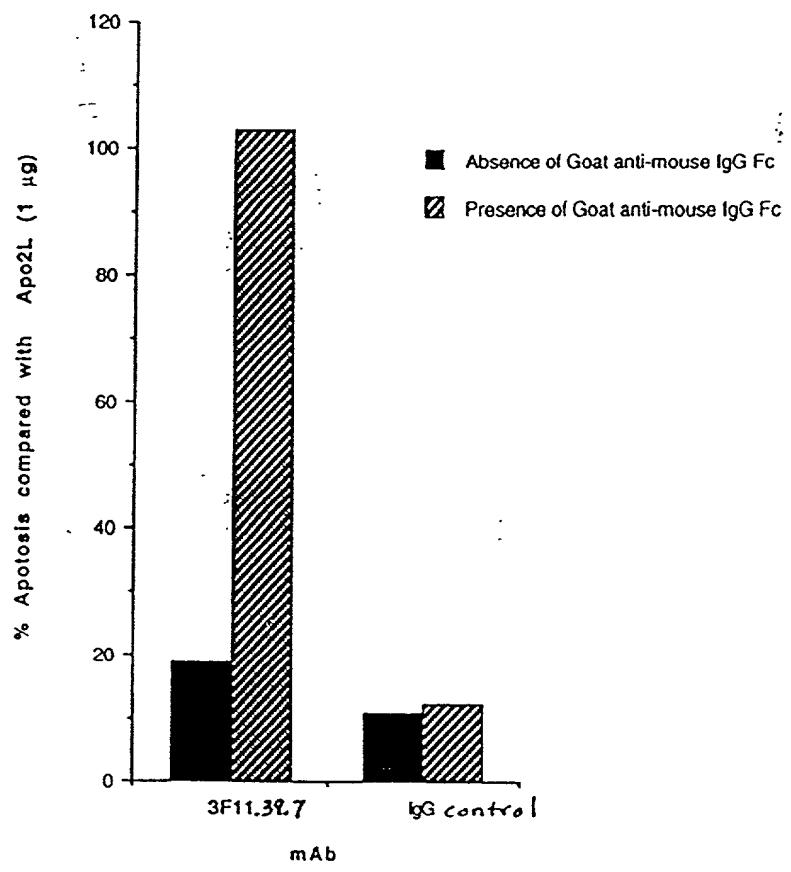


Fig. 9

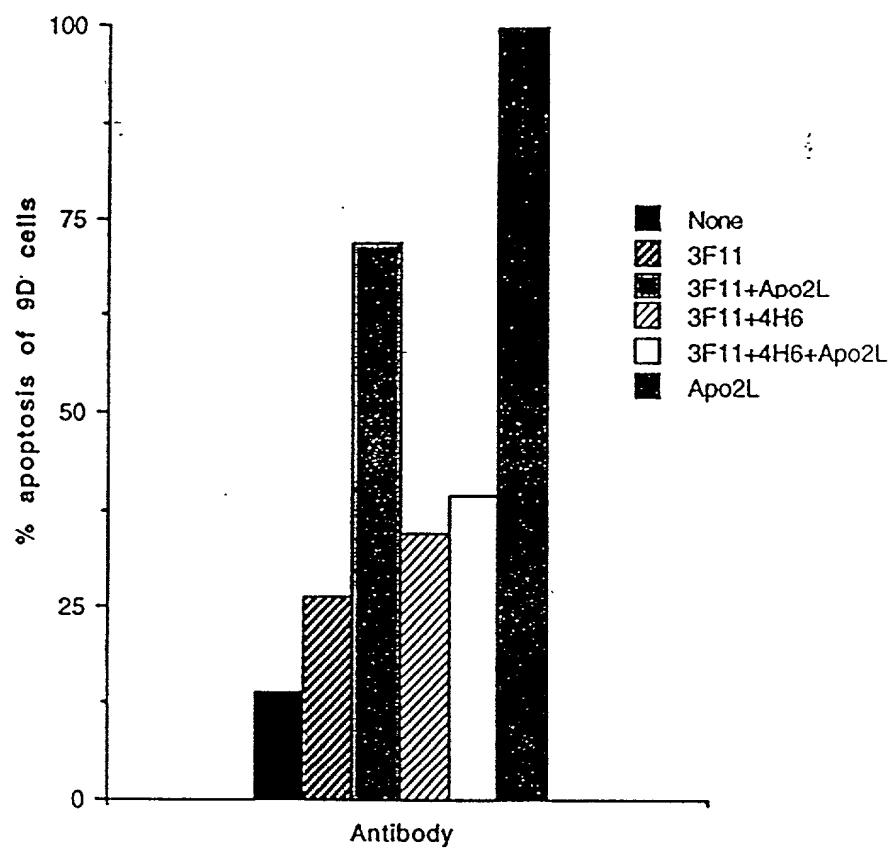


Fig : 10

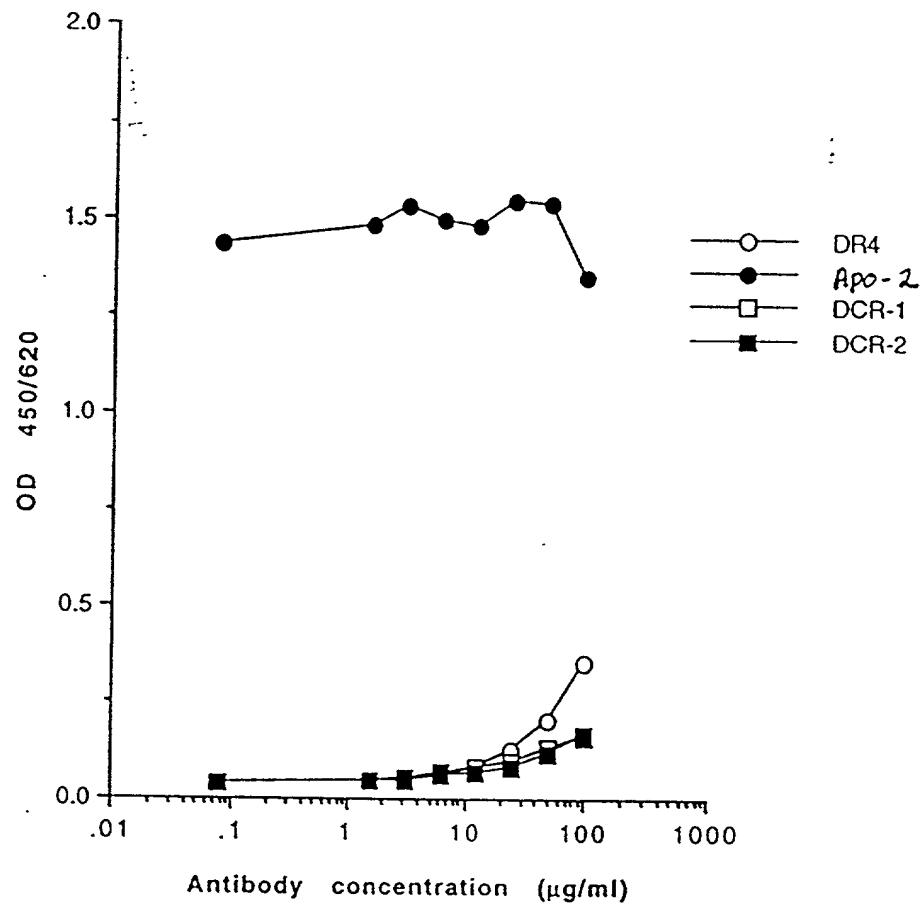


Fig. 11

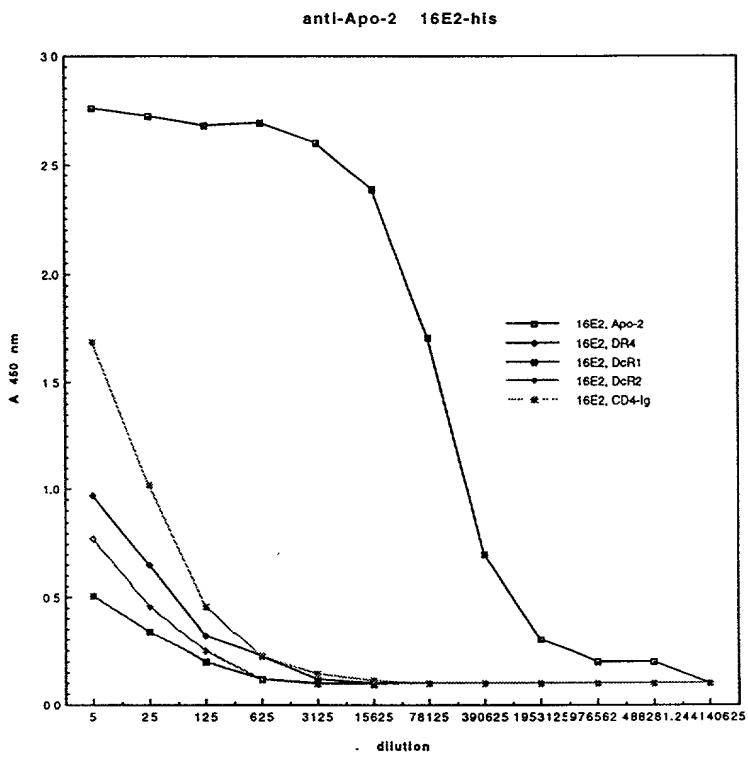


Fig. 12A

anti-Apo-2 20E6-his

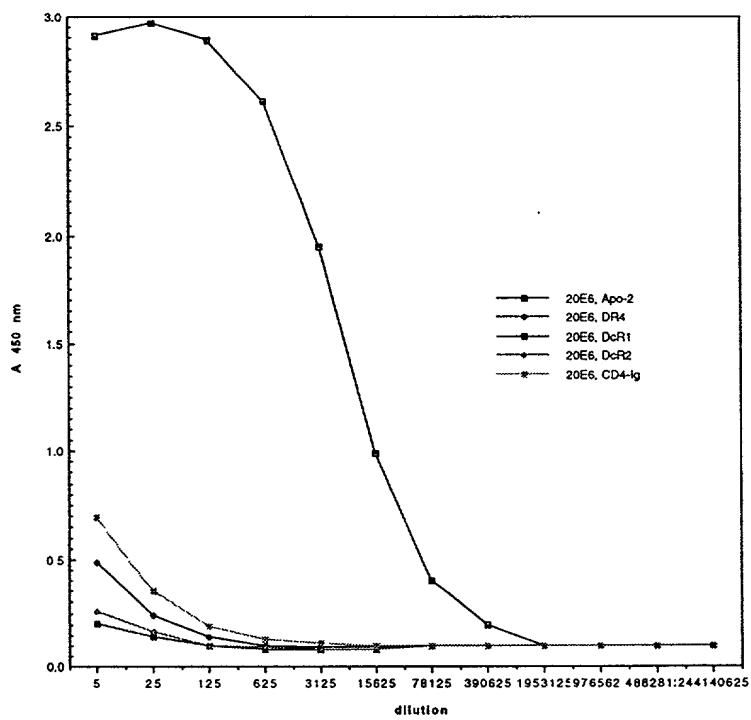


Fig. 12B

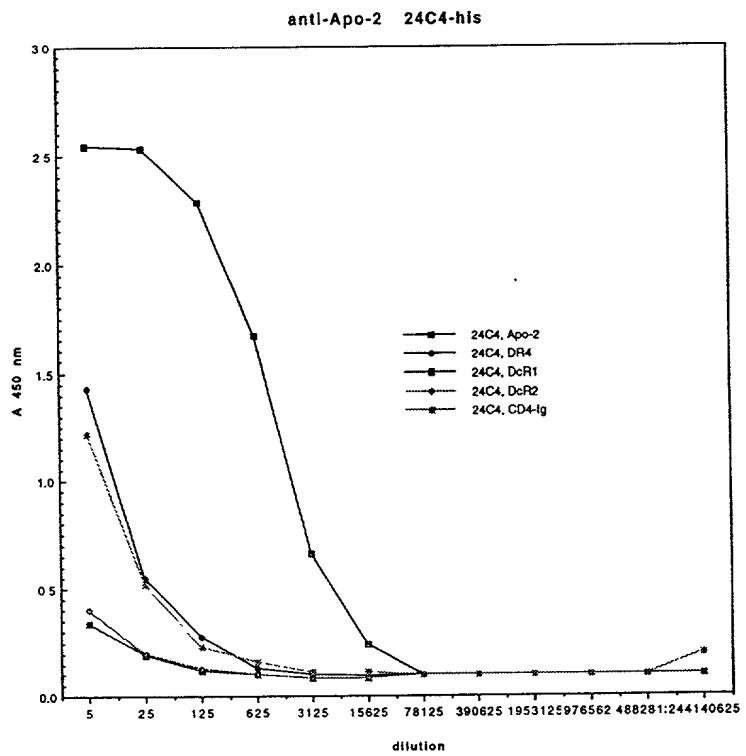


Fig. 12c

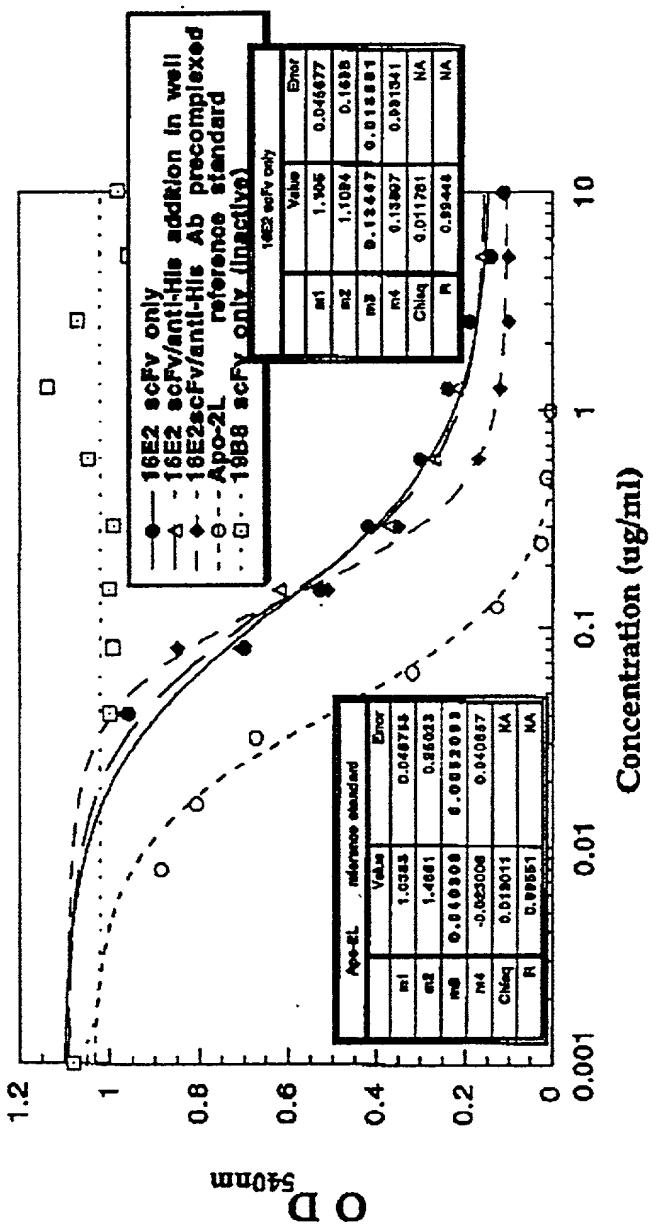


Fig. 13A

Fig. 13B

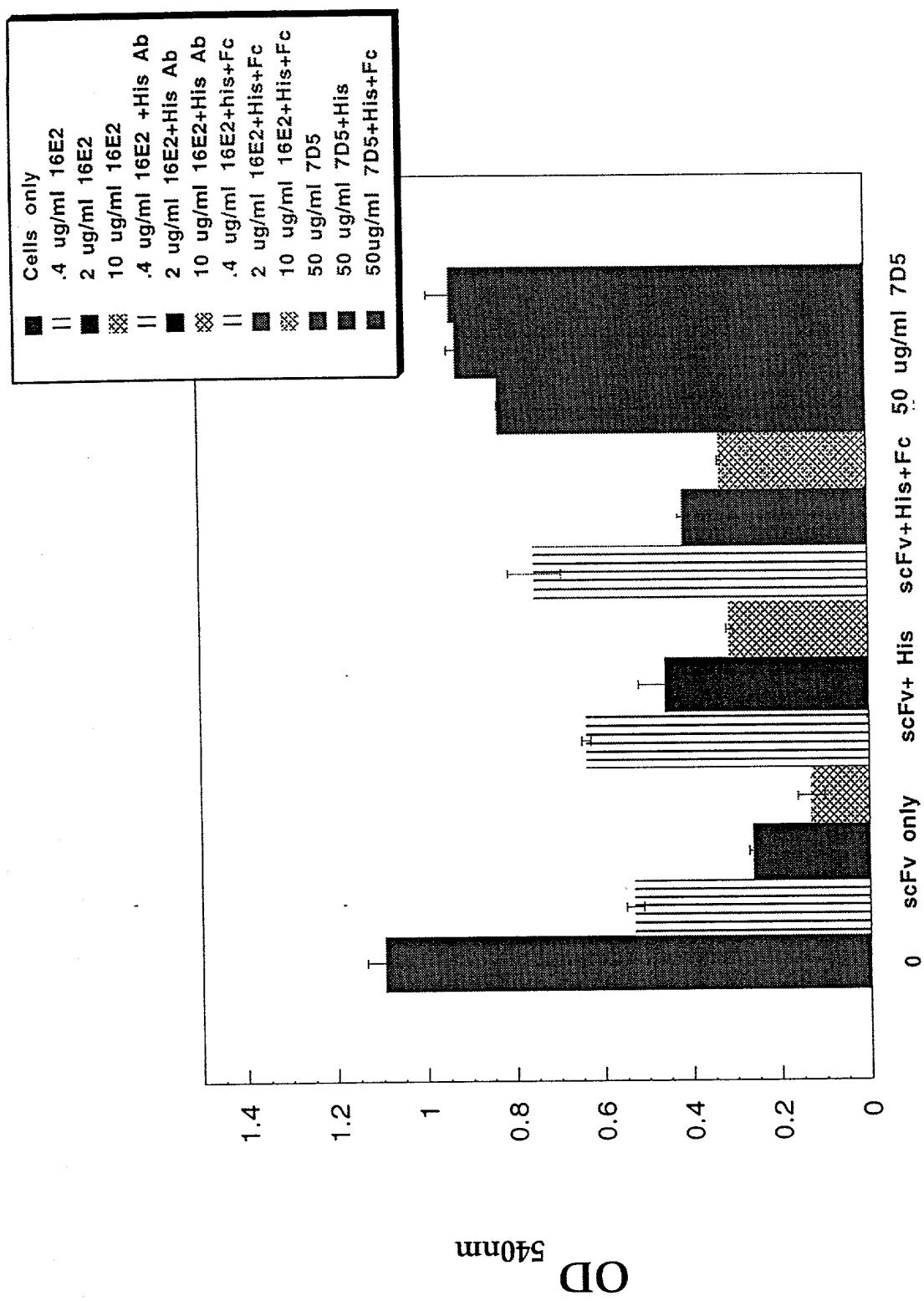
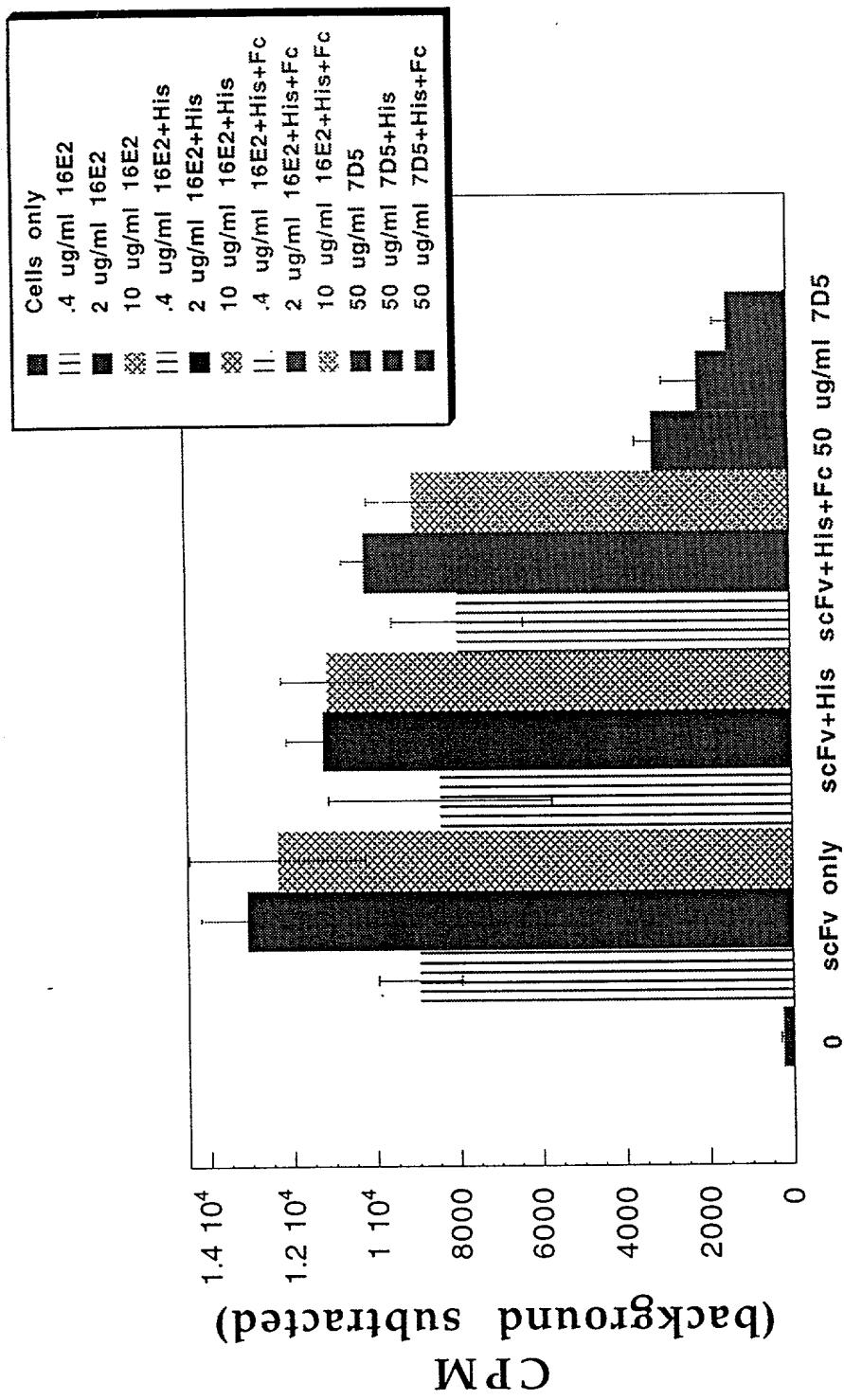
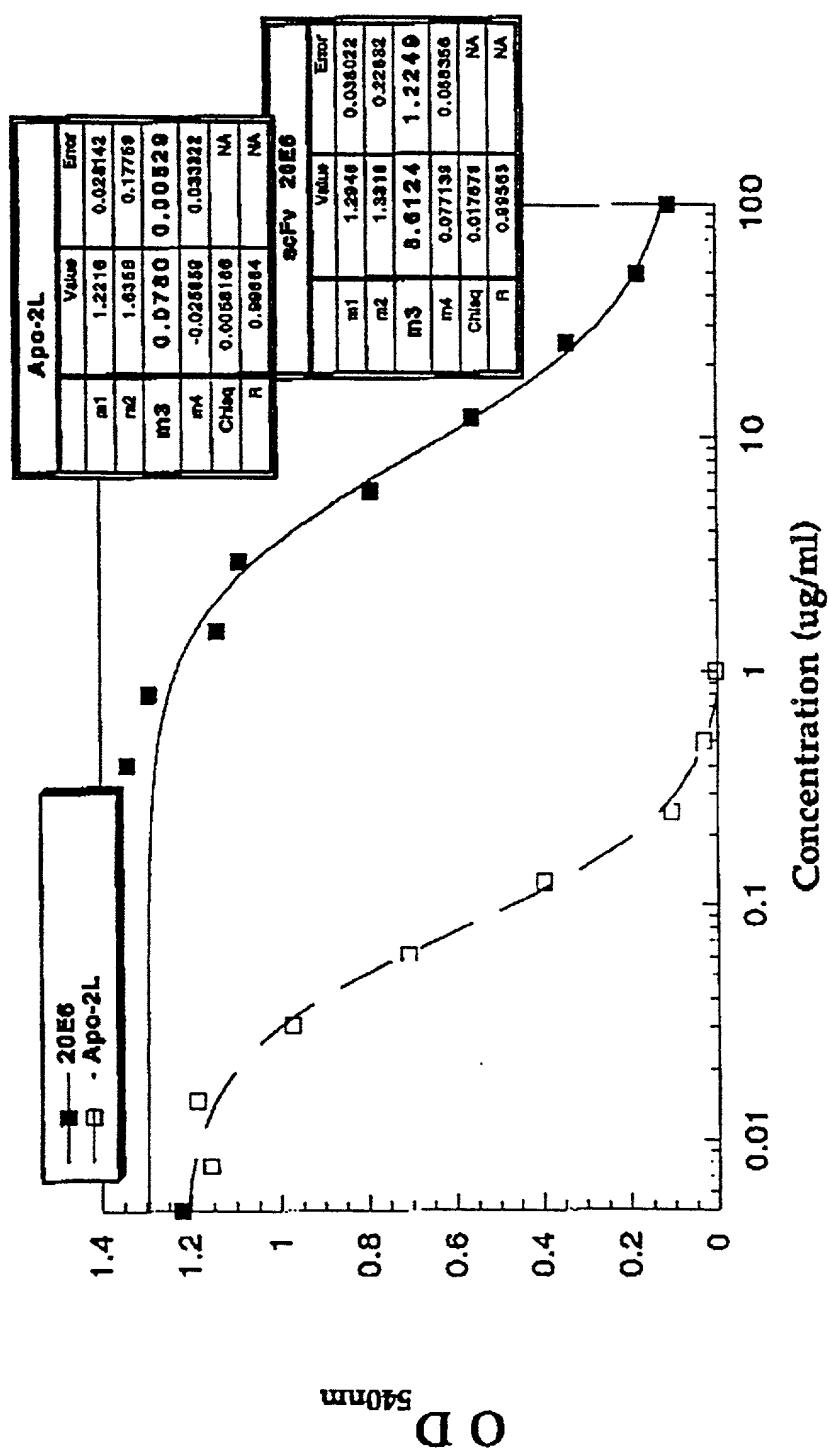


Fig. 13c



100 200 300 400 500 600 700



Concentration (ug/ml)

Fig 14A

Fig. 14B

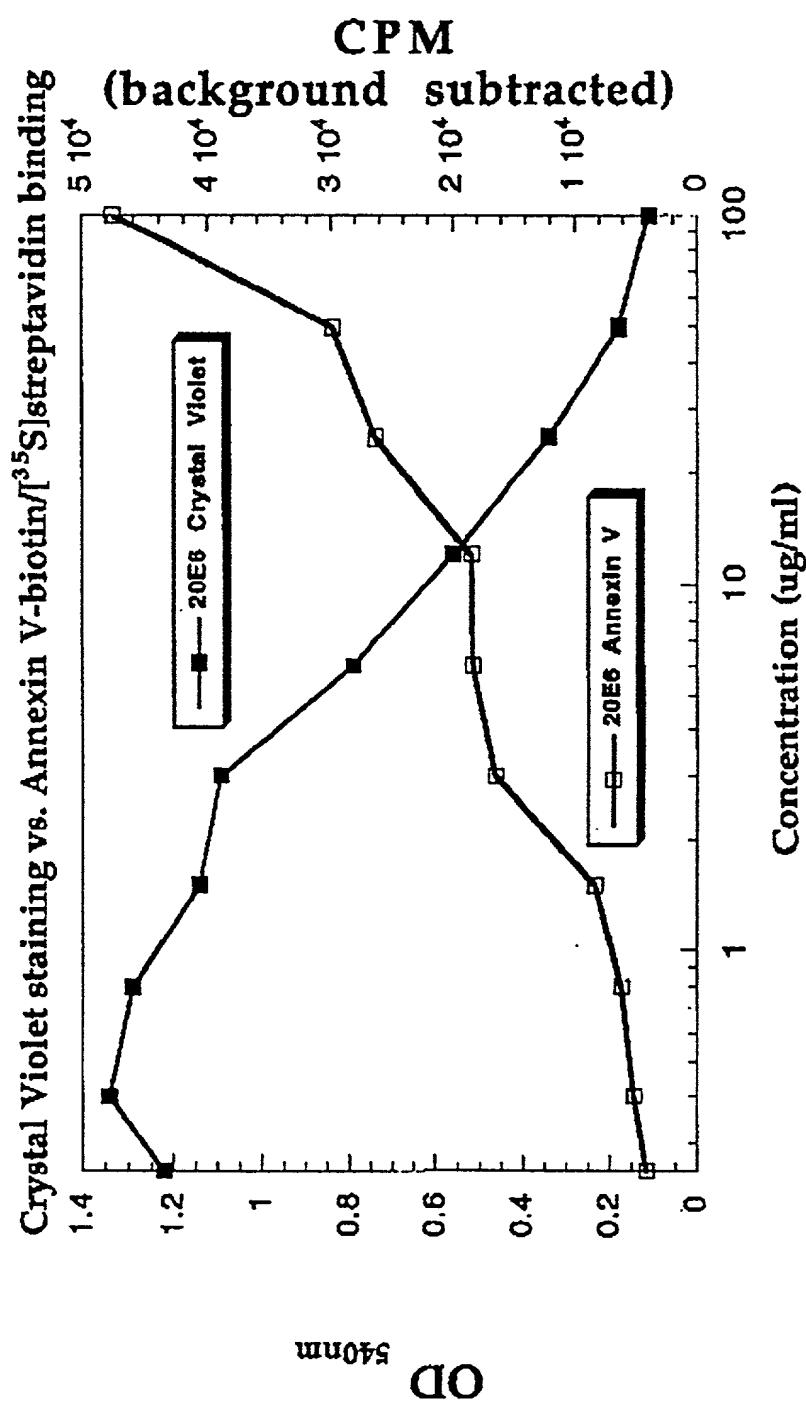
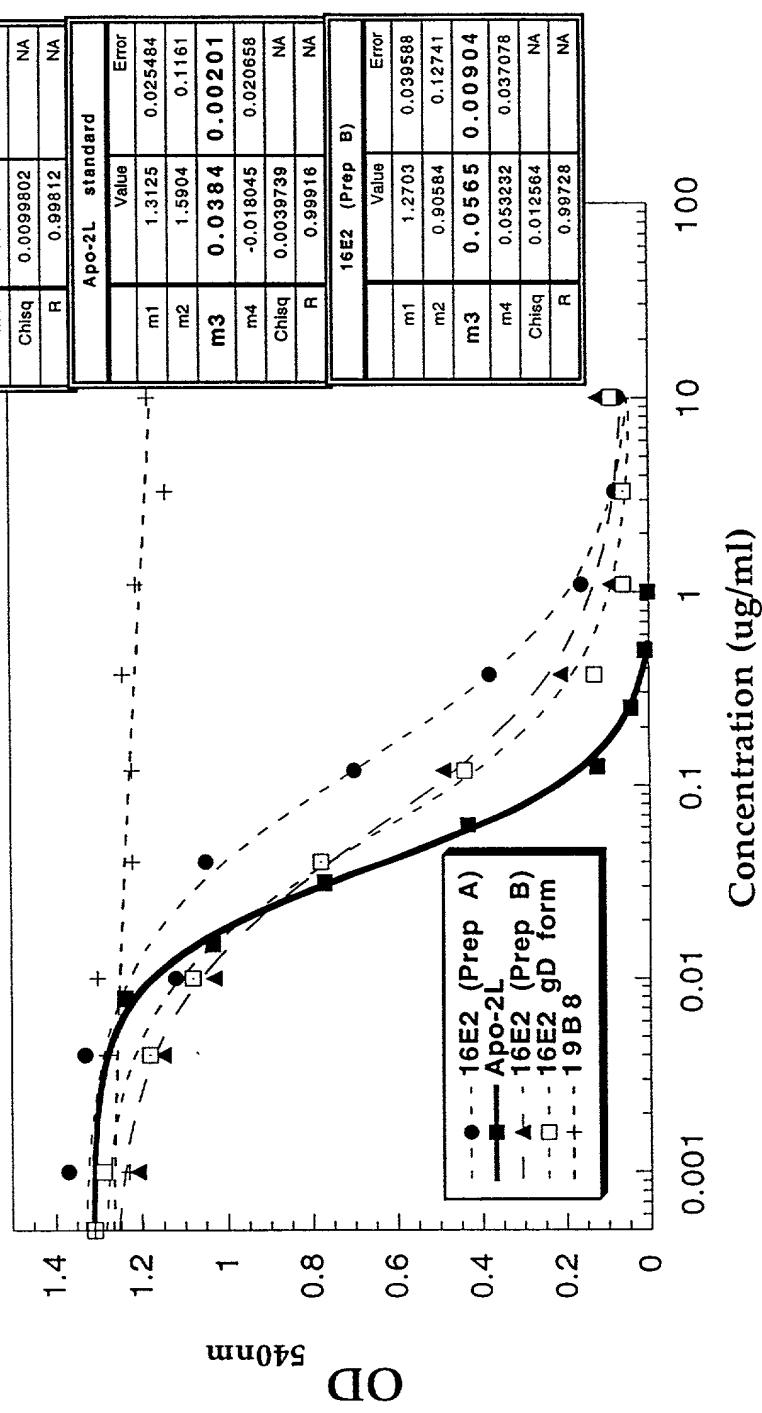


Fig. 14C



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ATGACCATGA TTACGCCAAG CTTTGGAGCC TTTTTTTGG AGATTTCAA 50
CGTGAAAAAA TTATTATTCTG CAATTCTTT AGTTGTCCT TTCTATGCGG 100
CCCAGCCGGC CATGGCCGAG GTGCAGCTGG TGCAGTCTGG GGGAGGTGTG 150
GAACGGCCGG GGGGGTCCCT GAGACTCTCC TGTGCAGCCT CTGGATTAC 200
CTTTGATGAT TATGGCATGA GCTGGTCCG CCAAGCTCCA GGGAAAGGGC 250
TGGAGTGGGT CTCTGGTATT AATTGGAATG GTGGTAGCAC AGGATATGCA 300
GACTCTGTGA AGGGCCGAGT CACCCTCTCC AGAGACAACG CCAAGAACTC 350
CCTGTATCTG CAAATGAACA GCCTGAGAGC CGAGGACACG GCCGTATATT 400
ACTGTGCGAA AATCCTGGGT GCCGGACGGG GCTGGTACTT CGATCTCTGG 450
GGGAAGGGGA CCACGGTCAC CGTCTCGAGT GGTGGAGGCG GTTCAGGCGG 500
AGGTGGCAGC GGCGGTGGCG GATCGTCTGA GCTGACTCAG GACCCTGCTG 550
TGTCTGTGGC CTTGGGACAG ACAGTCAGGA TCACATGCCA AGGAGACAGC 600
CTCAGAAGCT ATTATGCAAG CTGGTACCAAG CAGAACCCAG GACAGGCC 650
TGTACTTGTC ATCTATGGTA AAAACAACCG GCCCTCAGGG ATCCCAGACC 700
GATTCTCTGG CTCCAGCTCA GGAAACACAG CTTCCCTGAC CATCACTGGG 750
GCTCAGGCGG AAGATGAGGC TGACTATTAC TGTAACCTCCC GGGACAGCAG 800
TGGTAACCAT GTGGTATTCTG GCGGAGGGAC CAAGCTGACC GTCCTAGGTG 850
CGGCCGCACA TCATCATCAC CATCACGGGG CCGCAGAACAA AAAACTCATC 900
TCAGAAGAGGG ATCTGAATGG GGCCGCATAG 930

Fig. 15A

ATGACCATGA TTACGCCAAG CTTTGGAGCC TTTTTTTGG AGATTTCAA 50
CGTGAAAAAA TTATTATTCTG CAATTCTTT AGTTGTCCT TTCTATGC GG 100
CCCAGCCGGC CATGGCCGGG GTGCAGCTGG TGGAGTCTGG GGGAGGCTTG 150
GTCCAGCCTG GGGGGTCCCT GAGACTCTCC TGTGCAGCCT CTGGATTAC 200
CTTTAGTAGC TATTGGATGA GCTGGGTCCG CCAGGCTCCA GGGAAAGGGC 250
TGGAGTGGGT GGCCAACATA AAGCAAGATG GAAGTGAGAA ATACTATGTG 300
GAECTCTGTGA AGGGCCGATT CACCATCTCC AGAGACAACG CCAAGAACTC 350
ACTGTATCTG CAAATGAACA GCCTGAGAGC CGAGGACACG GCTGTGTATT 400
ACTGTGCGAG AGATCTTTA AAGGTCAAGG GCAGCTCGTC TGGGTGGTTC 450
GACCCCTGGG GGAGAGGGAC CACGGTCACC GTCTCGAGTG GTGGAGGCGG 500
TTCAGGCGGA GGTGGTAGCG GCGGTGGCGG ATCGTCTGAG CTGACTCAGG 550
ACCCTGCTGT GTCTGTGGCC TTGGGACAGA CAGTCAGGAT CACATGCCAA 600
GGAGACAGCC TCAGAAGCTA TTATGCAAGC TGGTACCAAGC AGAAGCCAGG 650
ACAGGCCCT GTACTTGTCA TCTATGGTAA AAACAACCGG CCCTCAGGGA 700
TCCCAGACCG ATTCTCTGGC TCCAGCTCAG GAAACACAGC TTCCTTGACC 750
ATCACTGGGG CTCAGGCGGA AGATGAGGCT GACTATTACT GTAACTCCCG 800
GGACAGCAGT GGTAACCATG TGGTATTCTGG CGGAGGGACC AAGCTGACCG 850
TCCTAGGTGC GGCGCACAT CATCATCACC ATCACGGGGC CGCAGAACAA 900
AAACTCATCT CAGAAGAGGA TCTGAATGGG GCCGCATAG 939

Fig. 15B

ATGACCATGA TTACGCCAAG CTTTGGAGCC TTTTTTTGG AGATTTCAA 50
CGTGAAAAAA TTATTATTCTG CAATTCTTT AGTTGTTCTT TTCTATGCCTG 100
CCCAGCCGGC CATGGCCAG GTGCAGCTGG TGCACTCTGG GGGAGGCCTG 150
GTCCAGCCTG GGCGGTCCCT GAGACTCTCC TGTGCAGCTT CTGGGTTCAT 200
TTTCAGTAGT TATGGGATGC ACTGGGTCCG CCAGGCTCCA GGCAAGGGC 250
TGGAGTGGGT GGCAAGGTATT TTTTATGATG GAGGTAATAA ATACTATGCA 300
GACTCCGTGA AGGGCCGATT CACCATCTCC AGAGACAATT CCAAGAACAC 350
GCTGTATCTG CAAATGAACA GCCTGAGAGC TGAGGACACG GCTGTGTATT 400
ACTGTGCGAG AGATAGGGC TACTACTACA TGGACGTCTG GGGCAAAGGG 450
ACCACGGTCA CCGTCTCCTC AGGTGGAGGC GGTCAGGCG GAGGTGGCTC 500
TGGCGGTGGC GGATCGCAGT CTGTGTTGAC GCAGCCGCC TCAGTGTCTG 550
GGGCCCCAGG ACAGAGGGTC ACCATCTCCT GCACTGGGAG AAGCTCCAAC 600
ATCGGGGCAG GTCATGATGT ACACTGGTAC CAGCAACTTC CAGGAACAGC 650
CCCCAAACTC CTCATCTATG ATGACAGCAA TCGGCCCTCA GGGGTCCCTG 700
ACCGATTCTC TGGCTCCAGG TCTGGCACCT CAGCCTCCCT GGCCATCACT 750
GGGCTCCAGG CTGAAGATGA GGCTGATTAT TACTGCCAGT CCTATGACAG 800
CAGCCTGAGG GGTCGGTAT TCGGCGGAGG GACCAAGGTC ACTGTCTAG 850
GTGCGGCCGC ACATCATCAT CACCATCACG GGGCCGCAGA ACAAAAACTC 900
ATCTCAGAAG AGGATCTGAA TGGGGCCGCA TAG 933

Fig. 15c

	signal	Heavy chain
Apo-2.16E2.his	1 MIMITPSFGAFFLEIFNVKKLLFAIPLVVPFYAAQPAMAEVQLVQSGGGV	
Apo-2.20E6.his	1 MIMITPSFGAFFLEIFNVKKLLFAIPLVVPFYAAQPAMAGVQLVESGGGL	
Apo-2.24C4.his	1 MIMITPSFGAFFLEIFNVKKLLFAIPLVVPFYAAQPAMAQVQLVQSGGGV	
		CDR1 CDR2
Apo-2.16E2.his	51 ERPGGSLRLSCAASGFTFDD <u>DYGM</u> SWRQAPGKGLEW <u>SGINWNGG</u> STGYA	
Apo-2.20E6.his	51 VQP P GGSLRLSCAASGFTFSS <u>YWM</u> SWRQAPGKGLEW <u>ANIKQDGSEKYY</u> V	
Apo-2.24C4.his	51 VQPGRSLRLSCAASGFIFSS <u>YGMH</u> WVRQAPGKGLEW <u>AGIFYDGGN</u> KYYA	
		CDR3
Apo-2.16E2.his	101 DSVKGRVTISRDNAKNSLYLQMNSLRAEDTAVYYCAK <u>IL</u> ---GAGR <u>WY</u>	
Apo-2.20E6.his	101 DSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR <u>DLLKVKGSSSGW</u>	
Apo-2.24C4.his	101 DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARD-----RGYY	
		Light chain
Apo-2.16E2.his	147 F-DLWGKGITVIVSSGGGGSGGGGSGGGGS-SELTQDPAVSVALGQT <u>VR</u> I	
Apo-2.20E6.his	150 F-DPWGRGITVIVSSGGGGSGGGGSGGGGS-SELTQDPAVSVALGQT <u>VR</u> I	
Apo-2.24C4.his	143 YMDVWGKGITVIVSSGGGGSGGGGSGGGGS <u>QSVLTQPPSVSGAPGQR</u> VTI	
		CDR1 CDR2
Apo-2.16E2.his	195 TC <u>QGD</u> SLR---SYASWYQQKPGQAPVLV <u>TY</u> GKNR <u>PSGI</u> PDRFSGSSSG	
Apo-2.20E6.his	198 TC <u>QGD</u> SLR---SYASWYQQKPGQAPVLV <u>TY</u> GKNR <u>PSGI</u> PDRFSGSSSG	
Apo-2.24C4.his	193 SCTGRSSNI <u>GAGHDV</u> WYQQLPGTAPKLL <u>TY</u> DDSNR <u>PSGV</u> PDRFSGSRSG	
		CDR3
Apo-2.16E2.his	242 NTASLTITGA <u>QAEDEADYY</u> CNSRDSSGNHW <u>FGGGT</u> KLTVLGA <u>AAHHHH</u>	
Apo-2.20E6.his	245 NTASLTITGA <u>QAEDEADYY</u> CNSRDSSGNHW <u>FGGGT</u> KLTVLGA <u>AAHHHH</u>	
Apo-2.24C4.his	243 TSASLA <u>ITGLQAEDEADYY</u> C <u>OSYDSSLRG</u> SV <u>FGGGT</u> KVTVLGA <u>AAHHHH</u>	
Apo-2.16E2.his	292 HGAAEQKLISEEDLN <u>GAA</u>	
Apo-2.20E6.his	295 HGAAEQKLISEEDLN <u>GAA</u>	
Apo-2.24C4.his	293 HGAAEQKLISEEDLN <u>GAA</u>	

Fig. 16